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10/521,387	01/14/2005	Reiner Luttmann	SARTORIUS-12	2344

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EXAMINER	
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1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,387	LUTTMANN ET AL.	
	Examiner	Art Unit	
	MICHAEL HOBBS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks submitted on 01/22/2010 has been considered by the examiner and entered for the record.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cornelissen et al. (CAB8-Compuer Application in Biotechnology, June 25-27, 2001) in views of Major et al. (*Biotechnology and Bioengineering*, vol. 34, pp 592-599, 1989) and Gruenberg et al. (US 2002/0138454 A1) and in further views of Lucido et al. (US 6,402,941) and Bartok et al. (US 6,599,735 B1).

6. Cornelissen teaches an integrated bioprocess for the production of recombinant proteins by cultivating Pichia Pastoris. For claim 1, Cornelissen discloses using a device that includes bioreactor that cultivates cells which is connected to an upstream feed receptacle or glycerol feed (Fig. 3) and to a downstream cross-filtration or micro filtration unit (Fig. 3, page 1 section 2 paragraph 5). The micro-filtration unit is has a retentate line connected to the bioreactor and a permeate line which connects to a product harvest vessel (Fig. 3). The process is monitored by various sensors which report back to a control unit (Fig. 4) where these sensors consist of pO_2 control, an off gas analysis and the use of an HPLC to determine glycerol level in the reactor (section 7 page 6 paragraph 2). Furthermore, this control is analyzer (Fig. 3) which is connected to an agitator control, but not to a pump. Also, Cornelissen does not teach a second harvest vessel connected directly to the bioreactor.

7. Major discloses a continuous fermenter for lactate production by *Lactobacillus delbreuckii* with partial cell recycle using a hollow-fiber ultra-filtration cartridge. For claim 1, Major discloses withdrawing a whole-cell culture from the fermenter by a

peristaltic pump that is upstream of a waste receiver or second harvest vessel (Fig. 1; page 594 second paragraph). It would be obvious to one of ordinary skill in the art to employ the step of using a waste receiver as suggested by Major in order to remove whole cells from the reactor of Cornelissen. The suggestion for doing so at the time would have been in order to maintain a constant volume in the fermenter (page 594 first paragraph lines 7-9). Major is silent regarding the analyzer being connected to the pump.

8. Gruenberg discloses a method of optimizing a bioprocess involving complex nutrient mixtures where there are several upstream reservoirs supplying culture medium to a bioreactor. For claim 1, Gruenberg discloses the step where the product is harvested into a vessel where the control to the pump is connected to a process computer via a RS-232 connection (Fig. 1). While not specifying that the motor is connected to an analyzer, the control unit (Fig. 1) is connected to the process computer and would indicate changes within the bioreactor that would initiate the pump to withdraw product from the bioreactor. Therefore, it would have been obvious to one of ordinary skill in the art to employ the process computer controlled pump as suggested by Gruenberg to withdraw whole cells from the fermenter of Cornelissen and Major with a reasonable expectation of success.

9. Both Cornelissen and Gruenberg disclose the step of having a sensor such as a dissolved oxygen sensor connected to an analyzer or control unit where, in the case of Gruenberg, the control unit is connected to and controls the motor on the pump (Fig. 1 of Gruenberg). Furthermore, Cornelissen and Gruenberg disclose sensors that

measure the metabolites of the cell culture, which are indirect measures of the cell concentration; they do not disclose the step of actually measuring the cell concentration within the bioreactor. The combined references of Cornelissen, Major and Gruenberg are silent regarding a cell concentration measurement step.

10. Lucido discloses an apparatus for the biological treatment of environmental contaminants and waste where the cell concentration of the microorganisms is determined by the turbidity of the solution. For claim 1, Lucido discloses the step of using an optical density sensor (sensor 22) to detect the turbidity of the solution where a higher turbidity reading in the bioreactor indicates a higher viable cell concentration (col. 6 lines 30-33). Lucido demonstrates another method used to monitor the extent of cell cultivation within a bioreactor using optical detectors instead of the metabolite sensors of Cornelissen and Gruenberg. Furthermore, the combined references demonstrate a need to monitor and control the cultivation within a bioreactor where the control means range from the metabolite sensors of Cornelissen and Gruenberg, the volumetric control of Major to the optical sensor of Lucido. The three methods perform the same task of monitoring the conditions within the bioreactor. Furthermore, these represent a finite number of methods for monitoring the conditions within the bioreactor and would have been known to one of ordinary skill in the art at the time of the invention. Therefore, following rationale E of *KSR*, 550 U.S. at ____, 82 USPQ2d at 1397, it would have been obvious to one of ordinary skill in the art to employ the step of using the optical sensor of Lucido within the control unit of Cornelissen, Major and Gruenberg with a reasonable expectation of success.

11. With regards to the step of using a second regulator for operating an upstream feed pump, Cornelissen discloses using a weigh control that receives a weight value, V_L, from a scale (Fig. 3) and compares this value with a reference value, V_{LW}, that is inputted into the weight control regulator (Fig. 3, page 3 section 4 paragraph 6). However, Cornelissen is silent regarding the step of having this regulator connected to a feed pump instead of a harvest pump. Major, Gruenberg and Lucido are silent regarding a second regulator controlling a feed pump.

12. Bartok discloses a continuous fermentation system that includes the step of using a fermentation vessel (vessel 1) and includes upstream vessels (vessels 2) that are used to store the nutrient solutions for the fermentation process. Further, the system includes two regulators or control systems (computer 7 and control unit 11) that monitor and steer the entire process. For claim 1, Bartok discloses using a control unit (unit 11) which is being broadly interpreted second regulator that monitors the process parameters from a control system (system 17) and further operates upstream feed pumps (pumps 3) in order to modify or control the dilution rate or pH of the system. The control unit (unit 11) is also connected to a scale (scale 4) that weighs the fermentation vessel (Fig. 1; col. 4 lines 43-61). Therefore, it would be obvious for one of ordinary skill in the art to employ the method of using the controller to operate an upstream feed pump suggested by Bartok within Cornelissen, Major, Gruenberg and Lucido with the predictable result of controlling the weight within the fermentation vessel.

13. With regards to claim 2, Cornelissen is silent regarding *in situ* sterilization of the process. For claim 2, Major discloses the step of sterilizing the hollow-fiber tube using

and associated tube work with a sodium hypochlorite solution before each fermentation run (page 594 paragraph 2 lines 1-3). This step of sterilizing the filter and tubes is being interpreted as an *in situ* sterilization. Furthermore, one of ordinary skill in the art would recognize the benefits of sterilizing the filter and tubes ahead of time and flushing the lines in the manner described above in order to prevent cross-contamination between the batches. Furthermore, the sterilization step of Major solves the problem of sterilizing the equipment used in the fermentation process without having to disassemble the entire apparatus between different fermentation runs. Therefore, following rationale A of *KSR*, 550, U.S. at ____, USPQ2d at 1396, it would have been obvious to one of ordinary skill in the art to employ the sterilization step as suggested by Major in order to sterilize and prepare the filter and bioreactor of Cornelissen for another run with predictable results.

14. However, Cornelissen and Major are silent regarding this process being controlled by a computer or controller.

15. Gruenberg discloses a process computer that controls the operation of the fermentation process, but does not mention using the processor to control the sterilization process of the bioreactor. However, it would be obvious to one of ordinary skill in the art to modify the sterilization process of Cornelissen and Major with the process computer of Gruenberg in order to automate the sterilization process so that it may be conducted *in situ* with a reasonable expectation of success.

16. For claim 3, Cornelissen teaches the step where the **valuable product** is recombinant proteins (Abstract). For claim 4, Cornelissen does not specify that the

process is conducted in a sequential and integrated manner, but does imply that the process steps happen in a specific sequence. Referring to Figure 1 of the OA, each phase of production leads to another phase which strongly implies that the production of recombinant DNA as taught by Cornelissen is sequential. Further, the automation of this process as shown in Figure 4 of Cornelissen shows that each part of the process is integrated or coupled and are part of the whole process (page 6 section 8 paragraph 1). Regarding the method of producing biotechnologically valuable products as in claim 5, Cornelissen teaches that the cells adapt to the medium and that the cells are propagated at a constant growth rate, μ, for the batch phase (page 3 sections 3 and 4, Fig. 2) and for claim 6 Cornelissen teaches the step of using an induction substance such as methanol during the production phase (page. 3 section 3 paragraph3) . For claim 7, Cornelissen teaches the step of using a flow diffusion analysis (FDA) to regulate a second feed receptacle (page 3 section 4, Fig. 3). With regards to claim 8, Cornelissen teaches that the product is harvested from the bioreactor by using a cross-flow filtration step (page 1 section 2 paragraph 5), but does not specify that the product is harvested cell-free. However, since the cross-flow filtration step filters out the recombinant DNA produced within the bioreactor, it is an intrinsic property of the product that it would be cell-free.

17. With regards to claim 9, Cornelissen teaches that the cell harvesting and media refreshing phase happen in parallel, but does not specifically teach that the retentate is harvested and that this step is followed by a medium refreshing phase. For claim 9, Major discloses the step of harvesting the whole cell mass or retentate from the

bioreactor as discussed above and further includes the step of controlling the dilution rate and recycle ration by two peristaltic pumps which is being interpreted as the medium replenishing step (page 594 paragraph 1 lines 12-16). It would be obvious to one of ordinary skill in the art to employ the step of refreshing the culture medium as suggested by Major in the cultivation process of Cornelissen. The suggestion for doing so at the time would have been in order to maintain a constant volume in the fermenter (page 594 first paragraph lines 7-9).

18. For claim 10, Cornelissen teaches the step of sending the retentate back into the bioreactor (Fig. 3) and sending the permeate from the filter to the product harvest vessel (Fig. 3).

19. Regarding claim 11, Cornelissen teaches the step where the yeast used to produce the **recombinant DNA** is Pichia pastoris (Abstract) and for claim 12, Cornelissen teaches the step where the inducing substance is methanol (page 3 section 4, Fig. 1 & Fig. 3). Regarding claims 13 and 14, Cornelissen teaches maintaining the methanol level at a constant level and that glycerol is fed to the bioreactor (page 3 sections 3 & 4, Fig. 3).

20. For claim 15, Cornelissen does not specify that the process is conducted in a continuous and integrated manner, but does imply that the process is continuous and integrated. Referring to Figure 1 of the OA, each phase of production leads to another phase which strongly implies that the production of recombinant DNA as taught by Cornelissen is continuous. Further, the automation of this process as shown in Figure 4

of Cornelissen shows that each part of the process is integrated or coupled with every step and device of the larger process (page 6 section 8 paragraph 1).

21. For claim 16, the fresh media refill and cell harvesting are carried out in parallel (page 3 section 4 paragraph 6).

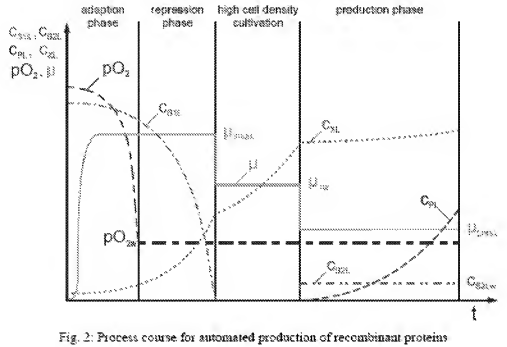

Fig. 2: Process course for automated production of recombinant proteins

Figure 1: Automated production of recombinant proteins (Cornelissen et al.)

22. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cornelissen et al. (CAB8-Compuer Application in Biotechnology, June 25-27, 2001) in views of Major et al. (*Biotechnology and Bioengineering*, vol. 34, pp 592-599, 1989) and Gruenberg et al. (US 2002/0138454 A1) and in further view of and Bartok et al. (US 6,599,735 B1).

23. Cornelissen teaches an integrated bioprocess for the production of recombinant proteins by cultivating Pichia Pastoris. For claim 17, Cornelissen teaches a device that includes bioreactor that cultivates cells which is connected to an upstream feed receptacle or glycerol feed (Fig. 3) and to a downstream cross-filtration or micro filtration unit (Fig. 3, page 1 section 2 paragraph 5). The micro-filtration unit is has a retentate line connected to the bioreactor and a permeate line which connects to a product harvest vessel (Fig. 3). The process is monitored by various sensors which report back to a control unit (Fig. 4) where these sensors consist of pO_2 control, an off gas analysis and the use of an HPLC to determine glycerol level in the reactor (section 7 page 6 paragraph 2). Furthermore, this control is analyzer (Fig. 3) which is connected to an agitator control, but not to a pump. Also, Cornelissen does not teach a second harvest vessel connected directly to the bioreactor.

24. Major discloses a continuous fermenter for lactate production by *Lactobacillus delbreuckii* with partial cell recycle using a hollow-fiber ultra-filtration cartridge. For claim 17, Major discloses withdrawing a whole-cell culture from the fermenter by a peristaltic pump that is upstream of a waste receiver or second harvest vessel (Fig. 1; page 594 second paragraph). This would be obvious to one of ordinary skill in the art to employ the waste receiver as suggested by Major in order to remove whole cells from the reactor of Cornelissen. The suggestion for doing so at the time would have been in order to maintain a constant volume in the fermenter (page 594 second paragraph). Major is silent regarding the analyzer being connected to the pump.

25. Gruenberg discloses a method of optimizing a bioprocess involving complex nutrient mixtures where there are several upstream reservoirs supplying culture medium to a bioreactor. For claim 17, Gruenberg discloses that the product is harvested into a vessel where the control to the pump is connected to a process computer via a RS-232 connection (Fig. 1). While not specifying that the motor is connected to an analyzer, the control unit (Fig. 1) is connected to the process computer and would indicate changes within the bioreactor that would initiate the pump to withdraw product from the bioreactor. Therefore, it would have been obvious to one of ordinary skill in the art to employ the process computer controlled pump as suggested by Gruenberg to withdraw whole cells from the fermenter of Cornelissen and Major with a reasonable expectation of success.

26. With regards to the second regulator for operating an upstream feed pump, Cornelissen discloses using a weigh control that receives a weight value, V_L, from a scale (Fig. 3) and compares this value with a reference value, V_{LW}, that is inputted into the weight control regulator (Fig. 3, page 3 section 4 paragraph 6). However, Cornelissen is silent regarding the regulator being connected to a feed pump instead of a harvest pump. Major and Gruenberg are silent regarding a second regulator controlling a feed pump.

27. Bartok discloses a continuous fermentation system that includes the step of using a fermentation vessel (vessel 1) and includes upstream vessels (vessels 2) that are used to store the nutrient solutions for the fermentation process. Further, the system includes two regulators or control systems (computer 7 and control unit 11) that

monitor and steer the entire process. For claim 17, Bartok discloses using a control unit (unit 11) or second regulator that monitors the process parameters from a control system (system 17) and further operates upstream feed pumps (pumps 3) in order to modify or control the dilution rate or pH of the system. The control unit (unit 11) is also connected to a scale (scale 4) that weighs the fermentation vessel (Fig. 1; col. 4 lines 43-61). Therefore, it would be obvious for one of ordinary skill in the art to employ the controller to operate an upstream feed pump as suggested by Bartok within Cornelissen, Major, Gruenberg and Lucido with the predictable result of controlling the weight within the fermentation vessel.

28. For claim 18, Cornelissen further teaches that the concentration of methanol is controlled by a feed pump that is connected to a control device (Fig. 3, page 3 section 4 paragraph 5) and for claim 19 the control device is a flow diffusion analysis (FDA) system (Fig. 3).

Response to Arguments

29. Applicant's arguments filed 01/22/2010 have been fully considered but they are not persuasive.

30. In the first paragraph on page 7, applicant summarizes the previous Office Action.

31. In the second paragraph on page 7 to the top of page 8, applicant argues that the applied reference of Cornelissen does not include the step of using an upstream pump

connected to a scale on the bioreactor. This is not found persuasive as this deficiency is corrected by the applied reference of Bartok.

32. Regarding applicant's argument in the first full paragraph on page 8, applicant further argues that Cornelissen does not disclose a second harvest vessel. This deficiency is corrected by the applied reference of Major.

33. Regarding applicant's argument on page 8 that the skilled artisan would not use the additional filter disclosed by Major nor look to the reference for the steps of waste removal, this is not found persuasive as Major corrected the deficiency within Cornelisson regarding the step of using a second waste vessel and the claim language does not preclude the step of using an extra filter.

34. Applicant further argues on the bottom of page 8 to the top of page 9 that Major does not disclose measuring the cell concentration or the upstream pump connected to a scale. The pump connection, as already stated, is corrected by the applied reference of Bartok.

35. Applicant's argument on the first full paragraph of page 9 is not found persuasive since the reference discloses the step of optically measuring cell concentration.

36. Applicant argues in the second paragraph on page 9 that the applied reference of Gruenberg does not render the instant claims obvious since it does not recite the steps of measuring and removing cell culture. This is not found persuasive as the Mettler balance used by the applied reference is connected to a process computer which operates the feed pumps upstream of the bioreactor. Furthermore, the regulator of the

instant application is an automatic controller which reads on the process computer of Gruenberg.

37. In response to applicant's argument that the applied reference of Gruenberg can not be combined with Major since the step of filtering happens after the removal of the reactor product, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

38. Applicant argues that the turbidity tester of Lucido is not the art equivalent of the cell concentration tester of the instant application in the third paragraph on page 10. This is not found persuasive as Lucido specifically states, as referenced in the action, that the optical density sensor detect the turbidity of the solution and that the higher the turbidity reading, the higher the viable cell concentration. While applicant may be their on lexicographer, it is unclear how this is not measuring cell concentration nor is it clear if applicant implies another method for measuring the cellular concentration within the bioreactor? Therefore, the sensor used by Lucido has been interpreted as the equivalent of the cell concentration sensor of the instant application.

39. Regarding the remarks in the first paragraph of page 11, applicant argues that there is no disclosure to combine the sensors of Lucido with the computer controlled

system of Gruenberg. This is not found persuasive as the courts have determined that it is obvious to automate a manual process (see also MPEP 2144.04 III).

40. Applicant further asserts regarding that the rejection of claim 1 is merely, as stated by the applicant, "conjecture, speculation and the assumption of undisclosed elements plus a hypothetical combination of multiple unrelated references cannot be grounds for an obvious rejection". The examiner disagrees with this characterization of the rejection of record and does not find this statement persuasive. It is also noted that "A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton."KSR, 550 U.S. at ___, 82 USPQ2d at 1397. "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle."Id. Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ."Id. at ___, 82 USPQ2d at 1396.

41. Applicant argues in the second paragraph on page 11 that the applied reference of Lucido is non-analgous art and that the skilled artisan would not have applied the reference. This is not found persuasive as Lucido demonstrates that the tubidity sensor as used was known at the time of the instant application and was known to solve the same problem of detecting cell concentrations within a reaction vessel. Furthermore, "A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton."KSR, 550 U.S. at ___, 82 USPQ2d at 1397. "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle."Id. Office personnel may also take into account "the inferences and creative

steps that a person of ordinary skill in the art would employ."Id. at ___, 82 USPQ2d at 1396.

42. Applicant argues that Bartok teaches away from removing filtered permeate and cell contaminated harvest. This is not found persuasive as the reference corrected the deficiency within Cornelissen regarding the regulator.

43. In the second paragraph on page 12, applicant argues that the combination references used in the rejection cannot be combined. This is not found persuasive. Applicant further argues that, basically, combining Cornelissen and Bartok with Major would destroy the references. In response to applicant's argument that, basically, combining Cornelissen and Bartok with Major would destroy the references, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

44. In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

45. Applicant's traversal of the rejection of claim 17 begins on page 13.

46. Applicant argues on page 14, that, regarding the Gruenberg reference, it is mere conjecture that the harvest pump is connected to a regulator/computer with sensors in

order to withdraw product from the reactor. This is not found persuasive as the applicant is mischaracterizing the reference. With reference to Figure 1 of Gruenberg, the harvest pump is connected to the process computer via a digital analog converter and a RS-232 connection. Further, the process computer is connected to a control unit via a RS-422 connection where this control unit is connected to both a dissolved oxygen sensor and a pH sensor. Based on the structural elements disclosed by Gruenberg, this is not mere conjecture as the disclosed apparatus is fully capable of performing this function.

47. Therefore, the rejection is proper and will stand.

Conclusion

48. No claims are allowed.

49. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL HOBBS whose telephone number is (571)270-3724. The examiner can normally be reached on Monday-Thursday 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/M. H./
Examiner, Art Unit 1797